

Case report

Sudden death due to cerebral malaria: A case report



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ABSTRACT

Malaria is generally diagnosed *ante-mortem*. Few *post-mortem* cases have been described in the literature. *Post-mortem* cases may present as sudden and unexpected deaths of young individuals rising suspicious of unnatural death, and may therefore be investigated by medical examiners. We present the case of a 24-year-old man who died a few days after returning from a trip to Mali (Africa). Death was attributed to cerebral malaria after a thorough *post-mortem* investigation. The pathological aspects underlying the fatal outcome are discussed.

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1. Introduction

Malaria is a parasitic disease. Eighty one percent of the cases come from African countries. In 2010, it affected 216 million people and is estimated to have caused the death of 1 240 000 people worldwide. Less than 10% people are affected out of Africa and the most frequent cases come from India.^{1,2} The number of people affected by malaria has increased since 1980, to a peak in 2004, particularly in Africa. In 2009, 2200 cases were reported to the French National Malaria Reference Centre, but the actual number of cases is likely to be around 3400. Among these cases reported in France, 90.4% contracted malaria in Africa, and 60.4% of these concerned travellers. More than 75% of cases reported in France involve people aged 15 to 60; 32.5% of the men were Caucasian and 64% were African, while 15.1% of the women were Caucasian and 82.2% were African.³

Imported malaria-related deaths are rare in developed countries. Classically, the diagnosis is established *ante mortem*. A few rare cases diagnosed *post mortem* have been reported in the literature.^{4–7} These all involved the sudden and unexpected death of

young individuals, and medical examiners were thus called on to investigate the cause of death.

2. Case report

We present the case of a 24-year-old man, who was found dead at home by members of his family. The level of decomposition indicated that death had occurred several days previously. Two weeks before the body was found, the man had returned from an annual trip to Mali. He had decided not to take anti-malaria tablets on this occasion for unknown reasons. During the trip, he travelled with a friend who contracted benign malaria, which was treated locally. Six days before the body was found, he visited his physician with flu-like symptoms, without neurological symptoms. In view of his recent trip to a malaria-endemic country, the physician prescribed an emergency blood test, which was not followed up by the patient.

With no other information explaining the young man's sudden death, the prosecutor ordered an autopsy.

The body weighed 78 kg and measured 178 cm in length. External examination showed no sign of violence. He had marbling, but he was not bloated. Autopsy revealed decomposition of the body, hepatomegaly (liver: 2043 g) and splenomegaly (spleen: 669 g), pulmonary oedema, and bilateral pleural extravasation, according to

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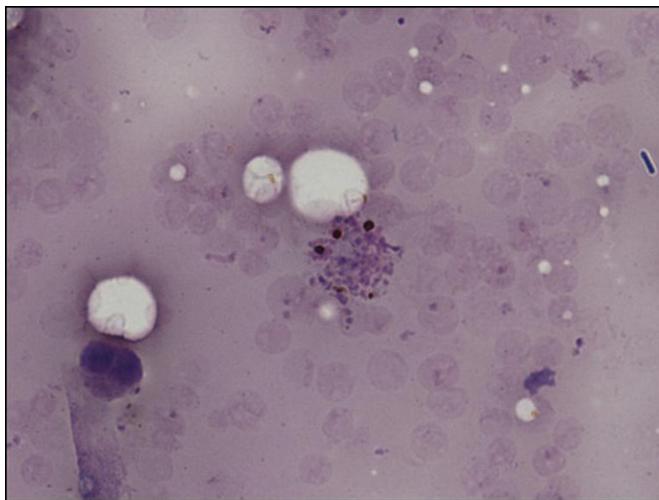


Fig. 1. Blood smear test – trophozoite and haemozoin ($\times 1000$ magnification).



Fig. 3. Brain section – dark granules of malarial pigment in parasitized erythrocytes of a small blood vessel (Hematoxylin Eosin Saffron stain, $\times 400$).

effusions fluid (right 350 ml; left 50 ml). The brain was removed intact and revealed a cerebral oedema, with the widening of the gyri and the narrowing of the sulci. A *post-mortem* blood sample was sent to the parasitology department. Despite the haemolysis, a blood smear test (Fig. 1) and a thick blood film (Fig. 2) revealed numerous parasite forms (trophozoite, schizont) suggesting *Plasmodium falciparum*. Malaria pigment was observed, in leucocytes and erythrocytes. An immunological test (ImmunoQuick Malaria+4®, AllDiag™) to detect malaria antigens revealed numerous *P. falciparum* HRP-II antigens. The diagnosis was confirmed by PCR analysis at the National Reference Centre for Malaria which detected *P. falciparum* DNA in the blood sample.

The neuropathological examination revealed malaria pigment in blood vessels, in each brain section examined (Fig. 3). The histopathological examination of liver and spleen revealed malaria pigment associated with cadaveric alteration (Figs. 4 and 5). The histopathological examination of the other major organs (heart, lungs, kidneys) revealed cadaveric alteration.

The toxicological tests were negative.

Death was attributed to cerebral malaria.

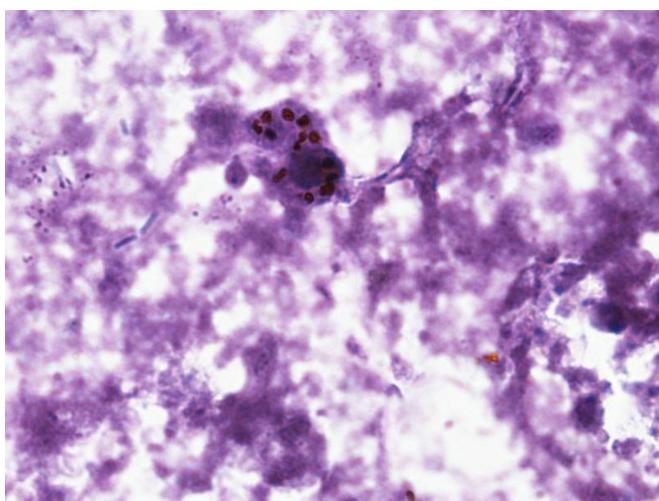


Fig. 2. Thick blood film – malarial pigment inclusions in a melanifer leukocyte ($\times 1000$ magnification).

3. Discussion

We present a rare case of a death related to malaria which had not been diagnosed prior to death. The victim had recently been to Mali, where *P. falciparum* is chloroquine-resistant. In 2009, 9.9% of all imported malaria cases in France originated in Mali.³ There is a lot of insufficient data regarding malaria transmission in Mali. What we know is that 90% of the population lives in high transmission area and these areas concern 10 to 50 per 1000 habitants confirmed malaria cases. In Mali, the number of cases has doubled since 1980, whereas this number has decreased in other sub-saharan countries.⁸

Cerebral malaria occurs when infected red cells induce microvascular thrombosis in cerebral vessels. The symptoms are those of acute febrile encephalopathy.^{7,9} Death follows in 33–100% of cases. The most frequent symptoms are seizure, mental confusion, and ultimately coma, usually followed by sudden death.^{4,7} Examination of the brain reveals oedema, congestion and white-matter petechial haemorrhages. Histological examination reveals parasitized erythrocyte sequestration, ring trophozoites, and deposition of birefringent hemozoin pigment.^{10,11} Splenomegaly and hepatomegaly are

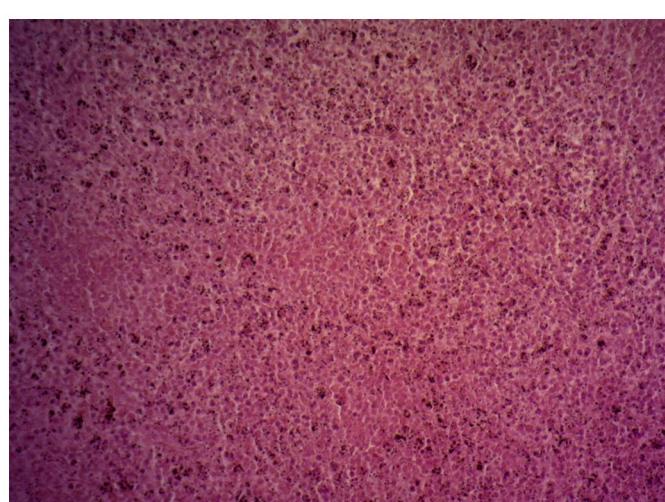


Fig. 4. Liver section – dark granules of malarial pigment in Kupffer cells ($\times 160$).

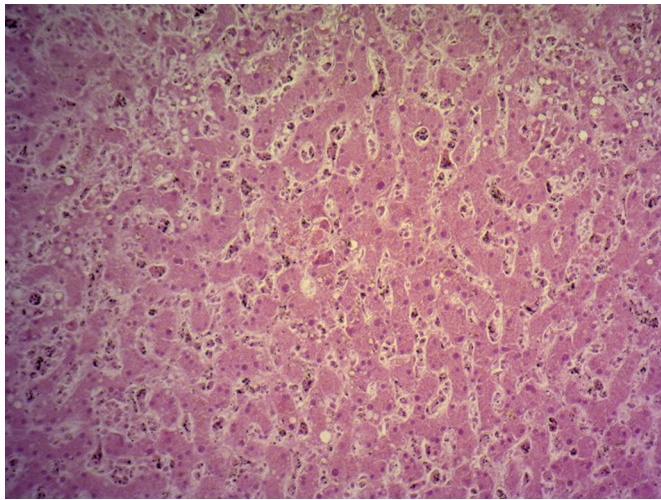


Fig. 5. Spleen section – dark granules of malarial pigment in the macrophages of the spleen ($\times 160$).

frequent and due to the obstruction of the lobular veins (liver) and the hyperplasia of the adenoid tissue (white pulp of the spleen).

Various hypotheses have been put forward to explain malaria pathophysiology. It is currently thought that parasitized erythrocytes bind to the endothelial cells, mediated by the tumour necrosis factor (TNF).^{10,12} When preventive treatment is not taken, the incidence of cerebral malaria is estimated to be between 44 and 77% of cases. *Plasmodium* is able to develop resistance to treatment.^{9,11} Travellers should therefore be made aware that intermittent stays in malaria-endemic countries do not provide immunisation.

In our case, the fatal outcome was rapid; the first symptoms appeared one week after the patient's return from Mali, and post-mortem examination revealed that death occurred shortly afterwards. The only neurological symptom found was a headache. It can not be excluded that other neurological symptoms have appeared after the medical examination, but had not been referred to anyone by the patient, who had only one medical examination. Our case is similar to the case described by Stoppacher et al., in 2003, mimicking influenza, without specific neurological symptoms, substantially identical with a timeline. Histopathological examination of brain section also found malaria pigments.¹¹ Peoc'h et al. described a cerebral malaria cases with gray discolouration over the temporal lobes in relation to an evolving chronic meningoencephalitis, confirming cerebral malaria because of black birefringent pigment associated to parasites consistent with *P. falciparum* in more than 90% of the brain sections examined. No clinical information prior to death was given in this case.⁷ In malaria related death, the fatal issue seems to be related to cerebral oedema.

Medical examiners may come across such cases when examining the sudden death of a young person, although they are rare as malaria is usually diagnosed *ante mortem*.^{4–7} Post-mortem diagnosis is difficult and neuropathological examination is required to confirm the neurological disease. Cerebral malaria cannot be

diagnosed only on the basis of neurological symptoms and para-sitaemia. Parasitaemia can occur without clinical signs.^{4,7,12} A recent trip to a malaria-endemic country must be taken into account, in view of the rapid fatal outcome.

This case report illustrates the fact that travellers, often through bad advice, fail to take preventive treatment when making frequent trips under similar conditions. Indeed increasing travel in malaria endemic countries and rapidity developing drug resistance, malaria will continue to be an important disease in developed countries.⁶ It also confirms the importance of informing travellers of the rapid fatal outcome, and hence of the need for early treatment and follow-up. It also indicates that infectious disease should be suspected in cases of sudden death, particularly when suggested by the clinical picture.

Ethical approval

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Conflict of interest

All the authors declare no conflict of interest.

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